The EurolInf study: A multicentre European comparative case control study of apomorphine versus intrajejunal levodopa infusion in advanced Parkinson’s disease

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On behalf of EUROPARK and the Movement Disorders Society Non Motor PD Study Group

Background

Intrajejunal levodopa infusion (IJL) and subcutaneous apomorphine infusion (Apo) are established treatments for advanced Parkinson’s disease (PD) although there are considerable differences in cost of treatment.

Methods

- 87 patients with advanced PD were assessed with
  Unified PD Rating Scale (UPDRS) III and IV, Non Motor Symptoms Scale (NMSS), PDQ-8 (Quality of Life Questionnaire) scores
- before initiation of therapy and after 6 months of therapy.

Results:

- Both groups were matched in terms of age, duration of PD, median H&Y stage, levodopa equivalency dose
- Effect size of both intervention on UPDRS III/IV and PDQ-8 scores were big (>0.8).
- Concerning the NMSS, differential effect was observed with sleep/fatigue and gastroenterological symptoms showing greater response to IJL, while mood was better improved with Apo with no worsening of hallucinations.

<table>
<thead>
<tr>
<th>Baseline vs. Follow-up</th>
<th>Relative change (%)</th>
<th>Effect size</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Apo</td>
<td>IJL</td>
<td>p*</td>
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<tr>
<td>UPDRS- Part 3</td>
<td>-43.26</td>
<td>-44.79</td>
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<tr>
<td>UPDRS- Part 4</td>
<td>-40.84</td>
<td>-56.06</td>
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NMSS Domains

Cardiovascular
-35.11 | -44.64 | NS | 0.25 | 0.41
Sleep/Fatigue
-23.56 | -48.23 | 0.017 | 0.40 | 0.73
Mood/Apathy
-47.00 | -24.75 | 0.003 | 0.49 | 0.30
Perceptual/Hallucinations
-53.97 | -49.79 | NS | 0.32 | 0.29
Attention/Memory
-33.98 | -25.60 | NS | 0.36 | 0.28
Gastrointestinal
-25.12 | -55.17 | 0.004 | 0.27 | 0.68
Urinary
-12.57 | -52.36 | 0.001 | 0.15 | 0.58
Sexual functioning
-24.61 | -59.51 | 0.001 | 0.12 | 0.43
Miscellaneous
-31.08 | -33.97 | NS | 0.39 | 0.54
NMSS Total score
-31.76 | -41.01 | NS | 0.53 | 0.83

PDQ-8 Summary index
-29.75 | -34.21 | NS | 0.89 | 1.14

Effect size: 0.2-0.49: small, 0.5-0.79: medium, ≥ 0.8: large
Moderate to large is desirable

Results effect size:

1. Motor effect
Both Apo and IJLI have large effect on UPDRS 3 and 4 but trend towards greater effect of IJLI on UPDRS 4 (1.69 vs 0.87, p=NS)

2. Non Motor effect:
- Sleep and fatigue: IJLI > Apo (0.73 vs 0.4, p=0.017)
- Mood and apathy: Apo > IJLI (0.49 vs 0.3, p=0.03)
- Autonomic (GIT/Urinary) IJLI >> Apo (Apo = small vs IJLI = moderate effect)
- Hallucinations: No worsening or reports with Apo or IJLI

3. Quality of life:
Large beneficial effect of Apo and IJLI: (0.89 vs 1.14, p=NS)

Conclusions:

First head to head real life multicentre comparative study of Apo infusion vs. IJLI in relatively matched advanced PD.
Both Apo and IJLI produce robust and significant improvement in motor and aspects of non motor functions in advanced PD and most importantly, quality of life.
However there are differences:
- IJLI causes greater dyskinesia reduction and has significantly better effect on gastrointestinal and genitourinary dysfunction
- IJLI leads to resolution of pre-existing ICD in some cases
- Apomorphine infusion has a greater effect on dysphoria and mood dysfunction and low rate of significant ICD development and no worsening or development of hallucinations/psychosis in the observation period.
- Side effects with IJLI need monitoring particularly: Demyelinating polyneuropathy (6.8%)
Weight loss and malabsorption syndrome (15.9%)